

Case report

Pseudogout, chondrocalcinosis and the early recognition of haemochromatosis

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Idiopathic haemochromatosis is a disorder which has a well-known association with chondrocalcinosis. We report arthritis associated with chondrocalcinosis as the first clinical manifestation of underlying haemochromatosis in two other-wise asymptomatic male patients. In one patient, pyrophosphate arthropathy presented with acute pseudogout. Better appreciation of this presentation will result in earlier diagnosis of haemochromatosis and the institution of appropriate treatment to prevent irreversible liver damage.

CASE 1. A 54-year-old man with no previous history of joint disease presented with an acutely swollen, painful left knee which had developed overnight. Plain radiographs of the knee demonstrated intra-articular calcification. Polarising microscopy of centrifuged deposit from the knee demonstrated typical calcium pyrophosphate dihydrate crystals. A diagnosis of pseudogout was made and indomethacin 25 mg three times daily prescribed. After six months there was persistence of the effusion in the left knee, and he also complained of episodic pains in his fingers, toes and both elbows. The metacarpophalangeal joints in both hands were enlarged with tender second and third metacarpal heads, lacking full flexion. Elbows had flexion deformities of 10 degrees but were not tender. All other joints including shoulders, cervical and lumbar spine were not tender, with normal range of movement. The liver was palpable below the costal margin, but the spleen was not palpable. Abnormal skin pigmentation was not present.

Radiographs of knees, wrists, pelvis and feet showed extensive cartilaginous calcification, including involvement of the second and third metacarpophalangeal joints of the hands (Fig 1). In the spine there was calcification within some intervertebral disc spaces and along the posterior spinal ligament. Fluid obtained from asymptomatic right and left knees contained typical calcium pyrophosphate dihydrate crystals.

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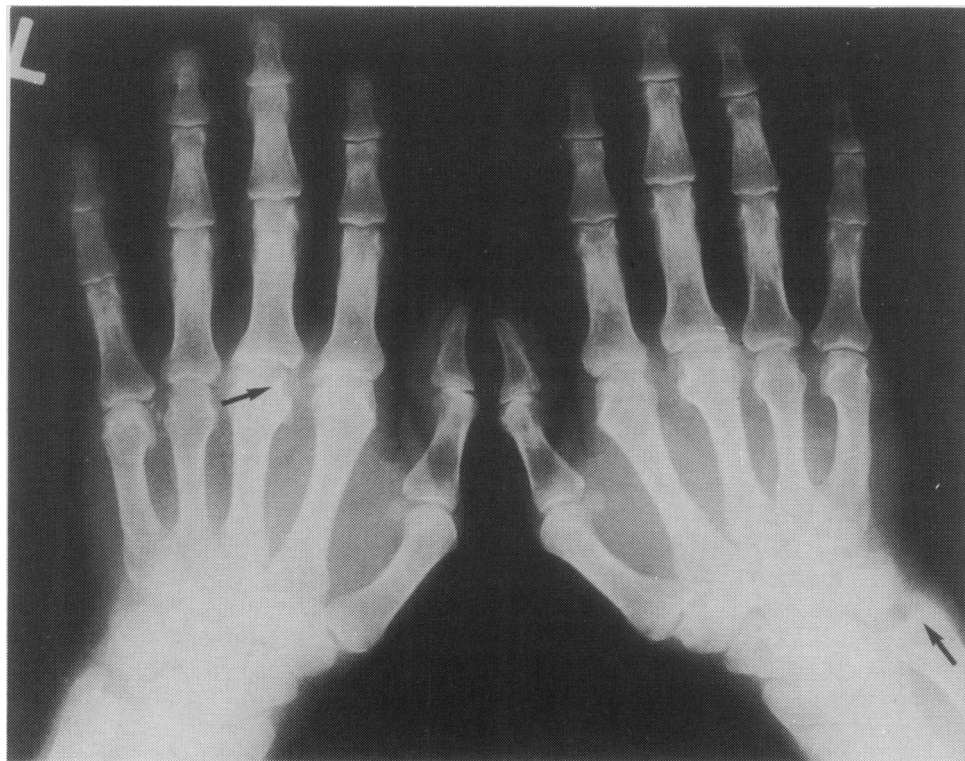


Fig 1. Case 1 — Calcification of wrist and third metacarpophalangeal joints.

Haemoglobin concentration was 15.5 g/dl, with a normal erythrocyte sedimentation rate and serum C-reactive protein. Plasma glucose was 8.2 mmol/l. There was moderate elevation of serum transaminases, a low plasma urea and a raised serum iron 68 $\mu\text{mol/l}$ (normal 14–29). Serum ferritin was also increased to 7920 $\mu\text{g/l}$ (normal 100–150). Transcutaneous liver biopsy showed extensive deposits of iron in hepatocytes by light microscopy with Prussian blue staining, and by electron microscopy. The concentration of iron by spectrophotometric analysis of liver tissue was 16.3 ng/kg dry weight (normal below 2.0). These results confirm the diagnosis of haemochromatosis.

His siblings (one male and three females) were screened, and plain radiographs, liver function tests, plasma glucose and full iron studies were entirely normal in all. The patient was venesected weekly, with a reduction in serum ferritin to 3080 mg/ml after 15 months. His joint symptoms have not returned although radiological calcification remains.

CASE 2. A 63-year-old male first presented in 1975 with pain and stiffness of the neck, shoulders, hands, hips and knees of two years duration. Examination showed painful limited movements of these joints. There was bony swelling of hands and knees with bilateral knee crepitus. Radiology showed cartilage loss and osteophytosis without chondrocalcinosis in hands, knees and feet. General examination was unremarkable apart from mild hypertension (170/100 mmHg).

He had not taken alcohol for 15 years. Haemoglobin was 15 g/dl with normal indices and erythrocyte sedimentation rate 4 mm in the first hour. Plasma glucose was 5.8 mmol/l. Serum aspartate transaminase was 74 μ /l (normal 16 – 51), alanine transaminase 144 μ /l (normal 10 – 45) and alkaline phosphatase 193 U/l (normal 35 – 106). Serum iron was elevated, 48 μ mol/l. Antinuclear antibodies, antimitochondrial antibody and anti-smooth muscle antibody were not detected in the serum. He was treated with indomethacin and salicylate for joint pain and cyclopentazide and potassium for hypertension.

On examination in 1985 the liver was 2 cm enlarged, smooth and non-tender without splenomegaly. He had painful limitation of movements of hips, knees, elbows, shoulders, wrists and fingers. There was a small effusion in the right knee and bilateral knee crepitus with bony enlargement of knees, wrists and finger joints. Radiographs of hips, knees, feet and lumbar spine showed widespread degenerative arthritis and chondrocalcinosis of the knee joints (Fig 2) but not the spine. Microscopy of synovial fluid from the right knee revealed typical calcium pyrophosphate dihydrate crystals. Haemoglobin was 15.7 g/dl and erythrocyte sedimentation rate 3 mm/hr. A glucose tolerance test showed mild diabetes mellitus. Serum alkaline phosphatase was still high at 387 U/l, but aminotransferases and gammaglutamyl transferase were normal. Serum iron was 46 μ mol/l,

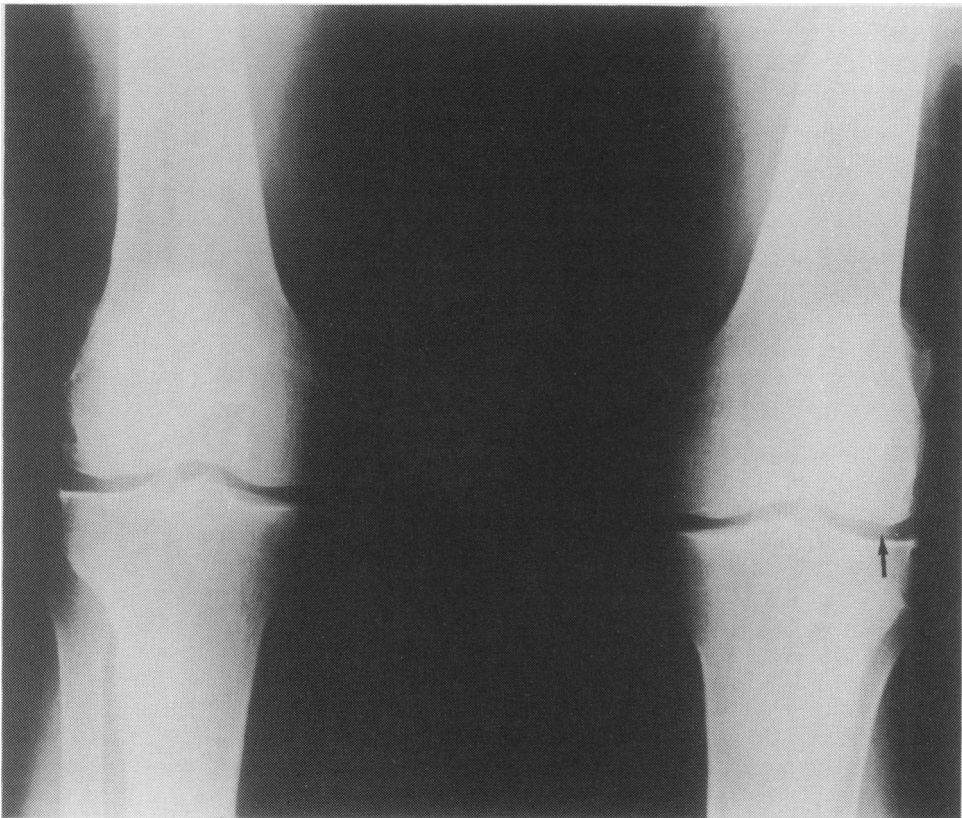


Fig 2. Case 2 — Chondrocalcinosis of the knees.

total iron binding capacity 54 $\mu\text{mol/l}$ (normal 46–72), with 76% saturation. Serum ferritin was 3423 $\mu\text{g/l}$. A desferrioxamine excretion test showed increased urinary iron elimination over 24 hours from 2 μmol to 19 μmol indicating considerable iron overload. Ultrasound scan of the liver showed increased echogenicity and decreased penetration consistent with fatty degeneration or early cirrhotic change. Computerised tomographic scan of the liver gave an attenuation value of 75 Hounsfield units (normal 60–70), just below a diagnostic range for haemochromatosis.¹ Needle biopsy showed extensive iron deposition in hepatocytes with normal liver architecture and membrane-bound haemosiderin deposits on electronmicroscopy. The concentration of iron per dry weight liver was 10.1 ng/kg confirming a diagnosis of haemochromatosis. Screening of the patient's siblings (two male and three female) was undertaken as in Case 1 and revealed no abnormalities. The patient was venesected weekly.

DISCUSSION

The relationship between chondrocalcinosis and calcium pyrophosphate dihydrate crystal deposition was first described by McCarty et al² and association with other diseases have been reported.^{3, 4} In a series of patients with haemochromatosis Schumaker described two patients with small and large joint arthropathy due to these crystals.⁵ The incidence of this arthropathy in haemochromatosis is now thought to be between 30 to 50% and of these over half have radiological evidence of chondrocalcinosis. The severity of the arthropathy, however, correlates poorly with the degree of iron overload and liver involvement and has even presented after prolonged venesection.^{6, 7}

Two previous reports have described four patients who subsequently had a diagnosis of haemochromatosis confirmed, where an arthropathy was the presenting feature. These patients had a history of arthritis present for two to 27 years prior to identification of haemochromatosis. Though the distribution of the arthropathy involving spinal and peripheral joints occurs in other diseases associated with calcium pyrophosphate crystal deposition, the changes at the metacarpophalangeal joints are characteristic and highly suggestive of the chondrocalcinosis associated with haemochromatosis.^{7–10} Our first patient presented with an acute episode of pseudogout which has not been previously described as the presenting feature of haemochromatosis.

In patients with chondrocalcinosis where the distribution of the disease is suggestive, including those who present with pseudogout, estimation of serum iron, ferritin and aminotransferases should be performed leading if necessary to a desferrioxamine test, CT scan and biopsy of the liver.

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